

recombinantly engineered to express endoglin protein or Alk-1 protein encoded by an exogenously supplied polynucleotide, whereby expression of said endoglin or Alk-1 protein promotes TGF β signal transduction in said cells in response to a TGF β ligand a gene that is capable of inducing endothelial remodeling in the endothelial cells.

REMARKS

Claims 18-26 constitute the pending claims in the present application. Applicants cancel, without prejudice, claims 22 and 23. Applicants add new claims 24-26. Support for the subject matter of these claims is found throughout the specification. No new matter has been added. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1. Applicants note that the election of Group III is acknowledged. Claims 18-26 are currently under examination and claims 1-17 are withdrawn from consideration as being directed to a non-elected invention.
2. Applicants' amendment to the specification is believed to obviate the objection.
3. Claims 18-23 are rejected under 35 U.S.C. 112, first paragraph, as allegedly containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to practice the claimed invention. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

Applicants contend that the claims are enabled throughout their scope. The specification provides an extensive discussion of angiogenesis and vasculogenesis. Furthermore, the specification recites a number of examples of genes known to play a role in angiogenesis and vascular identity including Alk1, endoglin, elastin, ephrin-B2, EphB4 and CD34. Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants have amended the claims to more particularly point out the claimed subject matter. Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal of this rejection are respectfully requested.

4. Claims 18-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for allegedly failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicants traverse this rejection to the extent that it is maintained in light of the amended claims.

a. Claims 18-23 are rejected because the term "polynucleotide encoding a gene" allegedly renders the claims indefinite. The Office Action alleges that it is unclear whether recitation of "gene" is meant to refer to a protein or DNA. Applicants contend that one of skill in the art would readily appreciate that the phrase is meant to refer to a polynucleotide which encodes a protein, and accordingly one of skill in the art would understand the metes and bounds of the claimed subject matter. Nevertheless, to expedite prosecution, Applicants have amended the claims to provide further clarity. Applicants' amendments are not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal are requested.

b. Claims 18-23 are rejected over the recitation of "endothelial remodeling". Applicants contend that the specification provides extensive discussion of endothelial remodeling, and one of skill in the art can readily appreciate the meaning of this term in light of the specification. Nevertheless, to expedite prosecution, Applicants have amended the claims to describe the claimed subject matter without reference to this allegedly ambiguous term. Applicants' amendment in no way indicates acquiescence to this ground of rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Reconsideration and withdrawal are requested.

c. Claim 22 is rejected over recitation of the term "or both". Applicants contend that one of skill in the art would readily appreciate that a gene, for example a recombinant gene engineered to include an internal ribosome entry sequence (IRES), can encode more than one protein. Alternatively, one of skill in the art would readily appreciate that two proteins can be encoded by two separate pieces of DNA. Accordingly, Applicants contend that the skilled artisan would readily appreciate the metes and bounds of claim 22.

Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants hereby cancel claim 22. Cancellation of claim 22 is not in acquiescence of

the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Cancellation of claim 22 renders the rejection moot, and reconsideration and withdrawal is respectfully requested.

d. Claim 23 is rejected over the recitation of the term "one or more of". Applying similar logic to that employed in response to the rejection of claim 22, the office action alleges that it is "unclear whether the gene encodes one or more of the genes." As outlined in detail above, Applicants maintain that one of skill in the art would readily understand the claimed subject matter. Nevertheless, to expedite prosecution of claims directed to commercially relevant subject matter, Applicants hereby cancel claim 23. Cancellation of claim 23 is not in acquiescence of the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope. Cancellation of claim 23 renders the rejection moot, and reconsideration and withdrawal is respectfully requested.

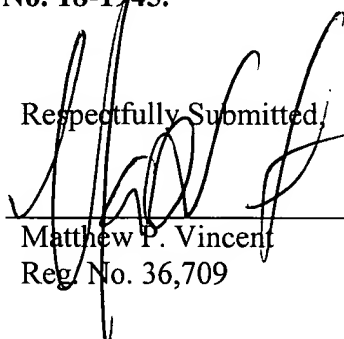
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Customer No: 28120
Docketing Specialist
Ropes & Gray
One International Place
Boston, MA 02110
Phone: 617-951-7000
Fax: 617-951-7050

Respectfully Submitted,



Matthew P. Vincent
Reg. No. 36,709